Label Comprehension, Self-Selection & Actual Use Studies: Issues & Challenges

Nonprescription Drugs Advisory Committee
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Andrea Leonard-Segal, M.D.
Director
Division of Nonprescription Clinical Evaluation

Center for Drug Evaluation and Research

Introduction

- Three types of studies are conducted to predict consumer behavior with OTC drugs
  - Label Comprehension Studies (LCS)
  - Self-Selection Studies (SSS)
  - Actual Use Studies (AUS)
- Lots of questions to raise about trial design and analysis
  - As a backdrop….we think studies are predictors of OTC consumer behavior but they have not been validated

Introduction

- Unlike results from randomized controlled studies where a drug can fail to demonstrate efficacy and/or safety….
  - Are there failed consumer studies?
    - Probably not
      - We can learn from results and apply them to make a better label

Content

- Labeling
- Label Comprehension Studies
- Self-Selection Studies
- Actual Use Studies
- Issues in Common
- Charge for Today
- Agenda

Labeling

Content of Drug Facts Label

- Information necessary for correct self-selection must be on Drug Facts label
- Lately we have seen OTC products and proposed OTC products for which the labeling is more and more complex
  - Cholesterol-lowering drugs
  - NSAIDs with new organ-specific warnings

Information Overload

- At what point do we pack so much information into the label that people stop reading it?
  - How should we determine what information must go on the Drug Facts label and what could go into package insert?
    - Information on inserts (leaflets) can be a condition of approval and are labeling subject to FDA regulation

Products with Package Inserts (Consumer Information Leaflets)

- Today Sponge (diagrams; expanded insertion directions)
- Vaginal anti-fungals (diagrams; expanded insertion directions; general information about vaginal infections)
- Nicotine replacement products (behavioral support and ways to decrease cravings)
- Plan B (expanded information about when and how to use; what to do if already pregnant, how to know if worked, mechanism of use)
- Proton pump inhibitors (tips to prevent heartburn, expanded drug information)

Label Comprehension Studies

Purpose and Issues

Purpose

- Test how well the label communicates information to the consumer
- Test ability of the consumer to apply label information in hypothetical situations in which the drug should or should not be used

LCS Measure Comprehension

- Understanding words does not necessarily predict decisions and actions
  - Good LCS results do not necessarily predict good AUS results
  - However, poor LCS results may predict poor results in AUS
  - Are there ways to improve the correlation between good LCS results and good AUS results?
    - The two types of studies usually enroll different populations (all comers vs. interested users)

Literacy

- OTC labels have been targeted to an 8th grade literacy level

- Populations enrolled in LCS
  - "General" population (normal + low literacy)
  - Enriched with more low literate participants (< 8th grade literacy)

Literacy

- Often has not been clear how to use the information on the low literate population
  - How should low literacy data be used?
  - Should the normal and low literacy populations be analyzed separately or en mass as one “general population?”

Literacy

- Does comprehension need to be the same for the normal literate and low literate populations?
- If not, what degree of difference is acceptable?
  - If 90% of the normal literacy population understands that a person with kidney disease should not take a drug, but only 70% of the low literacy population understands this, how should we act on this information?

Expectations of Comprehension

- What is a realistic expectation of consumer comprehension?
  - Often decisions about communication success come down to whether the comprehension level “feels good enough” to those interpreting the data
    - Do we expect too much?
    - Do we not expect enough?
- How do we determine what is adequate comprehension for a particular label communication element?
  - How do we know when to stop testing the label?
  - When have we achieved the most we can?

Studying the Label During LCS

- Study participants have unlimited time to study the label and can refer back to it as often as they wish during testing
- This is not “naturalistic”
  - Does this methodology inflate comprehension results?
  - Could this methodology be improved?
- Label comprehension testing that might require the participant to remember what is on the label (taking it away) is also not “naturalistic”

Interpreting Answers to LC Questions

- Common industry question: Are there answers not precisely “correct” as per the label information that could be considered “acceptable?”
  - Is comprehension “black” and “white?”
  - Should there be “acceptable” LCS responses?
    - How do we determine what is “acceptable?”
  - Industry often groups “acceptable” answers with “correct” ones. How should we analyze correct answers?

Scenario Question: Correct, Acceptable, or Incorrect

Label Warning: *Stop use and ask a doctor if you have abdominal pain.*

Scenario: *Sam is taking drug X. He develops abdominal pain. What should he do?*

Correct answer: *"Stop use and ask a doctor."*

Respondent's answer: *"Ask a doctor."*

- Not correct
- This is a default answer, but could be "acceptable."
- How should we interpret answers like this?

LCS Sample Size

- Industry often asks what an appropriate sample size is for the general population as well as for subpopulations
  - Usual study population approximately
    - 300 normal literacy
    - 150 low literacy
- It is unclear that these studies are always sized appropriately and we would like better clarity as to how to best populate these studies

Self-Selection Studies

Purpose and Issues

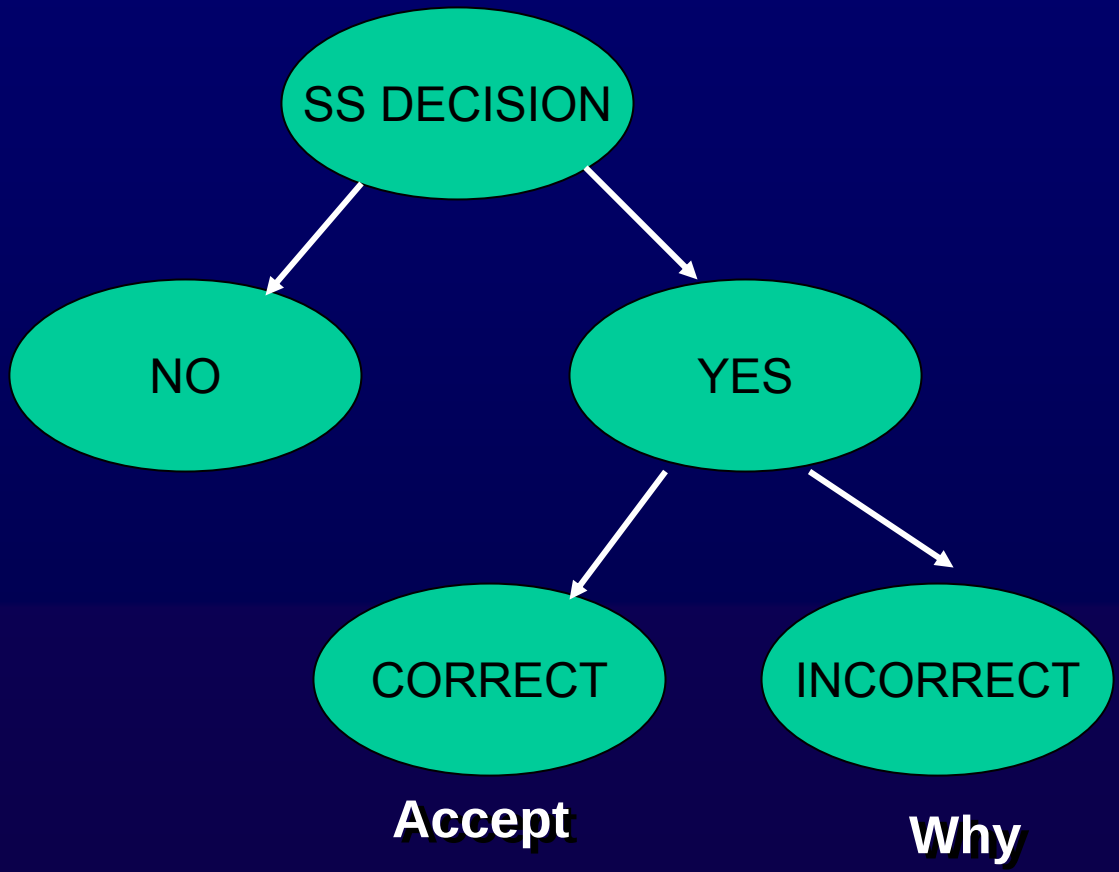
Purpose

- To determine if a consumer can correctly decide whether or not the product is appropriate for him/her to use based upon the label information
- SSS may be a stand alone study or be part of LCS or AUS

How to Pose the Self-Selection Question

- Is it appropriate for you to use this product?
  - It is not clear that we are asking the question the best way to acquire what we need to know
  - What is the best way to ask the SS question so as not to influence the respondent?

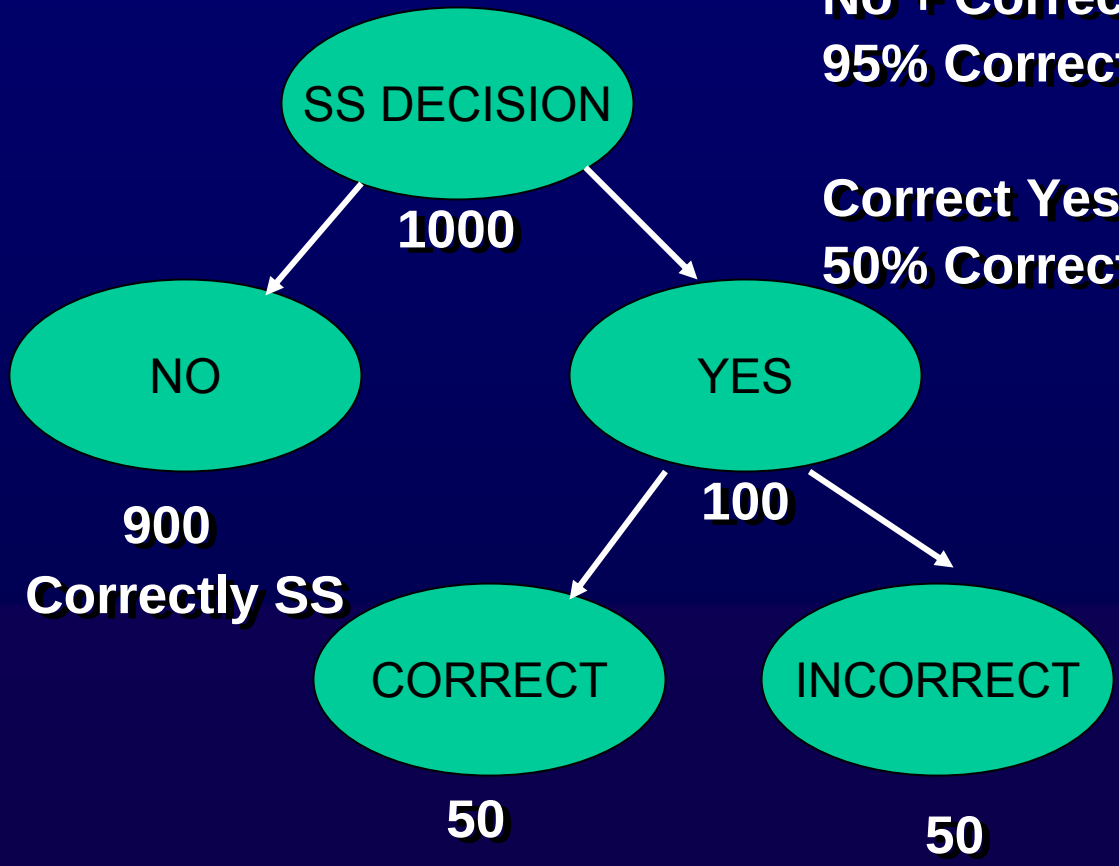
Self-Selection Decision Tree (What we have done)



Self-Selection Decision "No"

- Should we continue to disregard those who do not self-select to use the drug?
  - Should we only care about those who say "yes" because they will take the drug?
  - The "no" self-selectors could be correct in their decision

Self-Selection Decision Tree (Scenario)



No + Correct Yes = 95% Correct SS

Correct Yes = 50% Correct SS

SS Decision "Yes"

- When is "incorrect," in fact "acceptable" SS?
  - "Incorrect" SS decision to use a product for one person may be "acceptable" for another based on the individual's unique medical history
    - Cholesterol drug indication: Women > 55 years old
      - 40-year-old woman SS to use → "incorrect"
      - 40-year-old woman, status post hysterectomy whose mother died of MI age 36 → "acceptable"
      - Should this "acceptable" answer then be analyzed as "correct?"
  - Important to collect information about WHY consumers make self-selection "errors"
    - Often, sponsors do not

How Should We Interpret SSS Data?

- For a product label comprised of indication with many components and multiple warnings
  - Do participants need to weigh every piece of information correctly in their decision making?
    - Cholesterol lowering population
      - » LDL-C
      - » Total -C
      - » HDL-C
      - » Other Risk factors: Age, Hypertension, Smoking, Premature Fam Hx,
    - Warnings
      - » Pregnancy, liver, muscle, allergy, etc.

What We Have Done

- For cholesterol lowering drug we looked for the percent of perfect responders
  - < 5% perfect self-selection
- Was this too stringent an approach?

Analysis of SS Data

- Could we use different types of SS decision analyses?
  - Cumulative scoring of SS elements
    - Participant must achieve certain score by getting pre-defined # of elements correct
      - e.g., 5 out of 6
  - Pre-define a hierarchy of elements based upon risk/benefit
    - Must get certain elements correct: others optional
    - How would we prioritize?

Should We Verify The SS Decision?

- Verification can be difficult
- How aggressively should this be pursued?
  - For a cholesterol lowering drug, do we need to see lab data?
    - We did require this
  - Is self-reported information from study participants sufficient?
    - Do we need to confirm they spoke with a doctor?

SSS Sample Size

- Has been variable…
  - General population often tied to the sample size of the LCS or AUS
    - Has ranged from a few hundred to thousands
  - Subpopulation sample size
    - ~150 in study looking at teenagers
    - ~ 50 in studies looking consumers at risk for drug-drug interactions
- How should we determine the size of general population and subpopulations?

Actual Use Studies

Purpose and Issues

Purpose

- To simulate the OTC use of a product

- Can assess
  - Relationship between SS decision and purchase decision
  - Adherence
  - Safety
  - Efficacy in the OTC setting (seldom done)

Study Design

- Often have been single-arm, multi-center, uncontrolled, open-label
- Should we be considering other designs?
  - For example, how should we establish the benefit of educational materials?
    - Multiple arms comparing different communication tools and proposed marketing strategy
      - Labels
      - Educational materials vs. none

Purchase Decision

- After making a SS decision, consumers must decide whether to purchase the drug
- Sponsors often ask us to consider data on purchase decisions in AUS but we have been uncertain as to whether this is a good idea
  - Price influences purchase decisions
  - We cannot control the variability of drug cost
- Therefore, what is the relevance of considering the purchase decision of study participants?

Duration of Use

- How long should AUS go on?
  - Generally for a short term use OTC drug (i.e. analgesic), studies have been a week or two longer than the labeled duration of use
    - Is this appropriate?
  - For a chronic use drug, how should we determine an appropriate study duration?

Adherence in Actual Use

- We do not know what happens with Rx use of medication, although we generally assume it is “ideal” when compared with prospective OTC use
  - Patients are often noncompliant
  - Doctors sometimes prescribe the wrong drug (make a selection error)

Threshold of Adherence

- We do not want to set an unrealistic OTC standard for adherence
- How should we determine what our threshold should be for
  - Overuse or under use of study drug?
  - Adherence for chronic use product?

Issues in Common

Population Differences
Success and Failure Rates

- Should thresholds for success/failure for LCS, SSS, and AUS be the same across populations
  - if not, how do we determine the difference?
- When should the majority who could benefit from access to an OTC drug be denied that access because of SS errors made by a subpopulation at risk from drug use?

Analysis

- Results for general population and subpopulations have generally been analyzed to determine % correct responses for
  - Each communication objective in LCS
  - SS decisions
  - Actual use elements

Analysis

- Consideration needs to be given as to
  - Whether data should be presented other than as a point estimate (e.g., 95% confidence interval)
  - How these studies should be powered and the sample size calculated

Charge for Today

Generate new ideas for better consumer research for OTC drugs

Agenda

Health Literacy	Ruth Parker, MD Terry Davis, PhD
Consumer Behavior Studies	Saul Shiffman, PhD
Break	
Information Processing	Ruth Day, PhD
Statistical Considerations	Ralph D'Agostino,PhD
Complexities Rx to OTC Switch	Alastair Wood, MD
Questions from the Committee	
Lunch	
Open Public Hearing	
Break	
Committee Discussion	
Adjourn	